EXPANDED PROGRAMME ON IMMUNIZATION

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MEASLES CONTROL IN THE 1990's
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Summary

The Expanded Programme on Immunization has made significant advances in reducing morbidity and mortality from measles. Some countries in sub-saharan Africa with moderately high coverage levels have reported outbreaks in children outside the current target age group for immunization. Though these countries have succeeded in reducing overall measles incidence and mortality rates, the occurrence of outbreaks after a period of low disease incidence generates strong political and social pressure to respond, and risks a loss of confidence in the programme. The experience of immunization programmes in developed and developing countries are reviewed in this document, and recommendations are made about future directions of measles control in developing countries.

Major conclusions are that a period of low measles incidence is to be expected following the introduction of a mass immunization programme. This will be followed by a new pattern of recurrent epidemics, with a lengthened inter-epidemic period. Estimates from mathematical models of the percentage immunization required to achieve herd immunity do not mean that any one level of coverage will eliminate measles in all situations. Success of an immunization programme requires knowledge of the age and subgroup distribution of susceptibles and maximum effort to reduce their concentration throughout the community.

Outbreaks occur due to the accumulation of susceptible persons, both unimmunized children and vaccine failures. In developed countries, outbreaks in school-aged children are occurring principally among vaccine failures or clusters of children with exemptions from immunization. In developing countries, outbreaks in older children are occurring principally among children who have not been immunized and who have not been exposed to measles due to the reduced overall measles incidence. The role of vaccine failures in developing countries is difficult to assess due to poor documentation of immunization, especially among older children.

In large urban areas of developing countries, even with high coverage with current vaccines, the number of susceptibles may always be enough to sustain transmission, due to the high birth rate, crowding, and migration from rural areas with fewer immunization services. Measles remains endemic in these areas, with a large proportion of cases in infants less than 9 months of age.

High coverage must be achieved soon after the age at which children become susceptible to avert the maximum number of measles deaths. In developing countries, there is only a brief "window of opportunity" after maternal antibody has waned and before many children have acquired measles. In much of sub-saharan Africa, this is soon after 6 months of age.

Principal recommendations for developing countries are to increase coverage in young children and to develop the capacity to respond to outbreaks.

The current EPI recommendations for increasing coverage remain crucial to improve measles control. Priority should be given to urban and densely populated rural areas. Important measures to increase coverage are to use all health centre contacts to immunize children, establish a system to detect and refer defaulters from immunization services, and, in areas where overall coverage is high (70% or above), identify pockets of low coverage and target activities to them.

Information on immunization coverage and on disease trends is important to identify high-risk groups, monitor trends so that outbreaks can be anticipated, provide data to Ministries of Health, donors, and the public to show the progress made by the EPI; establish numerical targets for immunization activities and later for disease reduction and stimulate health workers to improve performance continuously. Actions to improve the collection, analysis and use of data on coverage, measles morbidity and mortality at all levels of the health care system are needed. Feedback should be given to health workers, administrative authorities and the community. These groups should be informed of the possibility of future outbreaks, which do not necessarily indicate programme failure. Health workers should be alerted to the fact that a prolonged interval free from measles does not mean that control has been achieved, and that is is important to try to identify and immunize clusters of susceptible persons.

Routine services should not be jeopardized by attempts to control outbreaks. Recommendations for outbreak investigation and control are therefore divided into minimum actions indicated in areas with few resources, and other, less essential actions and investigations. Each national programme should review the stage of development of immunization to determine how aggressively to promote outbreak control activities, and elaborate a checklist of actions for peripheral health workers to take when an outbreak is suspected.

Immunization programmes in developing countries are increasing coverage rapidly, with the result that measles epidemiology is constantly changing. Strategies for measles control need to evolve as the EPI matures. New high-dose vaccines may make a one dose schedule at 6 months of age a feasible option for many countries where measles in early childhood is common. A routine two-dose schedule may be considered in the future, to protect the small proportion of children who did not seroconvert after their first dose, to ensure lasting immunity, or to allow immunization of children under nine months of age until the newer generations of vaccines become widely available.

MEASLES CONTROL IN THE 1990s

1. Introduction

The Expanded Programme on Immunization (EPI) currently prevents over 1,350,000 deaths from measles in developing countries per year. Despite the success of the EPI, only 59% of children under one year of age were estimated to have received measles vaccine in 1988, and measles still causes an estimated 1.5 million deaths per year (UPDATE, EPI internal document 1989). The programme has a target of reducing the reported measles incidence by over 90% from pre-EPI levels, to below 40 cases per 100,000 population by 1995 (Henderson et al 1988).

In the early phases of the programme, the priority was to increase coverage in those children most at risk of severe measles, and WHO recommended that the target age group for immunization in developing countries be children 9-23 months of age. Recently, some countries with well-developed immunization programmes and measles vaccine coverage in the region of 70% have reported outbreaks of measles, some of which affected children outside the current target age group. This has prompted a reexamination of schedules and strategies for measles control.

This paper describes the epidemiology of measles in the pre- and post-vaccine eras in developed and developing countries, taking most examples from the USA and countries in Africa, where outbreaks have occurred for different reasons. Lessons learnt about measles control, both from experience to date and from mathematical models, are discussed. Recommendations are made for the improvement of measles control, with particular reference to the anticipated increase in outbreaks in older children in developing countries as their EPIs mature.

2. Measles epidemiology

2.1 Pre-immunization programmes

2.1.1 Developed countries

Before the introduction of measles immunization on a wide scale, measles incidence varied cyclically, with periodic epidemics occurring when the density of susceptible persons surpassed a certain critical level. In urban areas of the USA, the annual increase in cases in winter was punctuated by more severe epidemics every 2-5 years, each lasting approximately 3-4 months. A greater inter-epidemic interval occurred in smaller populations, where susceptible children accumulated more slowly, and therefore rural epidemics involved a broader age group (Mitchell and Balfour 1985). Schools were important foci for measles transmission; seasonal increases occurred, linked to the school year (Fine and Clarkson, 1982a).

The average age of infection was 4-6 years in most industrialized countries in the early 1960's, prior to the introduction of widespread immunization (Walsh, 1983). Anderson and May (1985) analysed measles reports from Europe and North America to estimate age-dependent rates of infection. They found that the

rate of infection rose approximately linearly in early childhood, peaked in the five-to-10 year old age group, and declined thereafter.

In developed countries, measles mortality fell long before the introduction of widespread immunization, probably due to reduced crowding (smaller families and improved housing conditions), better nutrition, and improved treatment. In the London fever hospitals in 1911-1914, measles case fatality among 9,277 admissions in the under-fives was 13.9% (Morley et al, 1963). In the early 1960's, only 12 deaths were reported among 50,000 reported cases in the UK (Miller 1964).

2.1.2 Developing countries

Measles trends differ in rural and urban areas. In urban areas, the pattern of alternate years of low and high incidence seen in developed countries prior to immunization may be less marked, because of the high birth rate and more rapid accumulation of susceptibles in developing countries. In Nairobi for example, epidemics occurred annually in the pre-immunization era (Hayden 1974).

Rural areas experience sporadic localized outbreaks with intermittent spread to adjoining regions depending on the amount of travel between regions. In a prospective community study in the Gambia, McGregor (1964) found that measles was absent from two villages for 12 years. A severe epidemic began after the introduction of measles to one village by a child returning from an area affected by measles, and the epidemic quickly spread to the other village. Outbreaks in rural areas in the pre-immmunization era affected persons of varying ages, depending on the length of time elapsed since the previous outbreak. They were often associated with high case-fatality ratios, as health care was not readily available (EPI 1979, 1985a, Kaartinen 1984).

Seeding of measles cases from endemic urban areas is considered to be an important source of measles transmission to rural areas (Davis 1982, Gordon et al 1965, Walsh 1983). In rural areas which have high population movement to and from surrounding areas such as towns or trading centres, measles epidemiology may resemble that in urban areas, with frequent introduction of measles causing small clusters of cases and shorter disease-free periods (Gordon et al 1965, Voorhoeve et al 1977).

Schools have played a smaller role in measles transmission in developing countries than in developed countries, as most children have acquired infection before school entry. Guyer (1976) found that for 6-23 month olds with measles, places of contact were a health centre (42%), a neighbour's house (28%), the home (15%), the grandparent's village (15%), or unknown (10%). For children aged 2-6 years, places of contact were a neighbour's house (78%), the home (28%), a health centre (6%), or unknown (11%). Klein-Zabban et al (1987) found health centres to be a major source of transmission in Abidjan, Ivory Coast.

In developing countries measles infects younger children than in developed countries, because of the high birth rate and often crowded living conditions. In addition, there is early loss of maternal antibody, probably due to reduced trans-placental concentration of maternal antibody compared with developed countries (Black et al 1986).

Children are infected at younger ages in urban than rural areas (Mitchell and Balfour 1985, Morley et al 1963, Walsh 1983) (figs 1,2). In urban Senegal, prior to immunization programmes, Baylet et al (1963) found that 50% of children acquired infection (assessed by seropositivity rates) by age 2 years and 88% by age 5 years. Boue (1964) found that 100% of urban children were seropositive at 18-24 months of age, whereas in rural areas 100% seropositivity was not reached until 10 years of age.

Table 1: Median age of incidence in community studies (adapted from Aaby, 1988a)

Africa	Age (years)	Immunization*	Reference
Rural			
Guinea-Bissau	3.5	No	Aaby 1984a
The Gambia	5	No	McGregor 1964
Senegal	3.5-5	No	Sy 1967, Pison 1988
Somalia	3.5	NI	EPI 1980
Kenya	2.5	Yes	Muller 1977
Urban			
Zambia	1.5	Yes	Rolfe 1982
Guinea-Bissau	2-2.5	No	Aaby 1984b, 1988b
Asia (rural)			
India	3-4	No	Salunke 1977, John 19 Agarwal 1986, Sinha 19
Afghanistan	6	No	Wakeham 1978
Burma	5	No	Chin 1985
Philippines	5	No	Almoradie-Javonillo 19
Bangladesh	3.5	No	Koster 1981

*Yes = immunizations carried out
No = no immunization
NI = no information

Case-fatality ratios (CFR) in developing countries are similar to those found in developed countries in the 1800's (Morley et al 1963). Community studies in Africa have shown CFRs varying from 3% to 15% (Table 2). Hospital-based studies give higher CFRs, due to selective admission of more severe cases. A 15% CFR was reported among children admitted to a hospital in Accra, Ghana, but community studies found a CFR closer to 3% (Morley et al 1963). CFRs vary depending on the age at infection, intensity of exposure, nutritional status, and availability of treatment.

Table 2: Case-fatality ratios for measles around the world (adapted from Walsh, 1983) From community studies, unless indicated by *.

Country	Year	Immunization	CFR(%)	Reference
Kenya	1976	Yes	6.5	Voorhoeve 1977
Gambia	1961	No	14.0	McGregor 1964
Gambia	1981	Yes	4.8	Williams 1983
Nigeria	1961	No	7.0	Morley 1963
Nigeria (war areas)	1968	NI	15.0	Smith 1970a
Ghana	1978	NI	3.0	Morrow 1981
India (Punjab)	1959	NI	1-2	Wyon 1971
India (Madras)	1969	Yes	1.5	Pereira 1972
India (Aurangabad)	1972	No	2.2	Shah 1972
Bangladesh	1976	No	3.7	Koster 1981
Chile*	1960	No	4.0	Ristori 1962
Guatemala	1963	No	4.5	Gordon 1965
USA (Prevacc)*	1961	No	<0.02	Langmuir 1962
USA (vaccine era)*	1975	Yes	0.01	Barkin 1975
USA (epidemic on Indian reservation)	1974	Yes	4.0	McCormick 1977
UK *	1963	No	0.02	Miller 1964

* = reported through routine surveillance.

Case-fatality ratios are higher among young children. In community studies in rural Guatemala, Gordon et al (1965) reported an 11.5% CFR in infants, 8.5% for one-year olds, 5.1% for all under-five year olds, and 3.7% for children aged 5-9. CFRs varied between villages, depending on the availability of medical care. In a community study in two villages in The Gambia, McGregor (1964) reported a CFR of 24% for children under five years, and of 11% for older children.

Table 3. Measles case-fatality ratio by age group (from Rodrigues, 1987).

Age in months	The Gambia		Guinea-Bissau		Ghana	
	%	N	%	N	%	N
0-5	0	2	0	3	16	181
6-12	78	9	34	29	20	1764
12-23	22	18			17	1690
24-35	18	17	10	63	13	419
36-48	13	23			10	137
>48	4	66	11	66	2	126
	Williams + Hull 1983		Aaby 1986		Commey+Richardson 1984	

%=% case-fatality ratio N=number of children with measles

In retrospective community studies in West Africa, Cantrelle (1964) found that measles mortality rates fell after 5 years of age (Table 4).

Table 4. Measles mortality rates per 1,000 per year by age group, retrospective community surveys in West Africa, 1957-1963

Age(yr)	Senegal*	Burkina Faso (Upper Volta)	Benin (Dahomey)
	Rural	Rural	Urban+rural
< 1	3.8-27.5	25.9	2.0
1-4 yr	9.9-24.2	24.7	3.8
5-9	2.2-2.6	5.9	0.6
10-14		1.4	

* 3 surveys were conducted.

Black (1982) used data from the Greenland epidemics of 1951-1962 to compare case-fatality ratios among young children who were not protected by maternal antibody, since the mothers had not had measles prior to the epidemics. The case-fatality ratio in infants less than one year old, 3.8%, was more than six times higher than that in children one to two years old and 53 times higher than children over two years old. Case-fatality ratios rose again in adults over 35 years of age, and in those over 55 years of age was slightly higher than in infants.

Studies which measure only acute case-fatality provide a minimum estimate of measles case fatality, as delayed deaths contribute to measles mortality (Aaby 1984b). Delayed excess mortality is greater when children contract measles before one year of age (Hull et al 1983, Osagie 1986, van de Walle 1986, Williams and Hull 1983).

2.2 The effect of immunization programmes on measles epidemiology

2.2.1 Developed countries

In the USA, measles immunization was introduced in 1963, but coverage was low until 1966, when the Federal government began to purchase and distribute vaccine. Though measles incidence fell markedly following the start of the immunization programme, incidence fluctuated over the first 10 years, as monies available for immunization varied. The United States Immunization Survey reported during the late 1970's that only about 67% of children aged 10-13 years were immunized. Other children had been incorrectly immunized and were also susceptible. In 1976 the reported number of cases rose to almost double that of the preceding 3 years (Mitchell and Balfour 1985). In 1978 a measles elimination programme was announced, with three major strategies: maintenance of high coverage; mandatory immunization prior to school entry; careful surveillance and aggressive outbreak control. These measures achieved a further drop in reported cases to an all-time low of 1,497 cases in 1983.

The age distribution of cases in the USA changed markedly after the immunization programme. Pre-immunization, only 10% of cases

were in persons over 10 years of age. In 1976, more than 60% of cases were in individuals over 10 years old, with 20% over 15 years old. It is important to note that though the proportion of cases in children over 10 years old increased, the incidence of disease in this age group decreased by 97% compared to the prevaccine era.

Measles elimination proved more elusive than anticipated. Though the USA was close to elimination of indigenous measles in the early 1980's, reported measles incidence has increased since 1982, despite over 97% of school enterers having proof of prior immunization. During 1985 and 1986, over 88% of reported cases occurred in 152 outbreaks (defined as the occurrence of 5 or more cases related epidemiologically). There were two major types of outbreaks: those in which most of the cases occurred among preschool children (age under 5 years) and those in which most of the cases occurred among school-age persons (age 5 to 19 years) (Markowitz et al 1989). A small proportion of outbreaks (7%) occurred among persons over 19 years of age.

Forty outbreaks (26 percent) occurred in preschool-age children; a median of 32% of cases were in children under the recommended age for immunization, and a median of only 14% were in appropriately immunized children. Preschool outbreaks accounted for 46% of total reported cases in 1986 and mainly occurred in poor inner-city areas. Most cases were in unimmunized children, and surveys of two-year old children in affected areas of inner cities found coverage levels of only 49-65 percent.

101 of the 152 reported outbreaks (67%) occurred primarily among school-age children. Attack rates in individual schools were low (1-5%), and the calculated vaccine efficacy was high. In many outbreaks, measles spread to persons in the community who were not of school age. In contrast to preschool outbreaks, school outbreaks occurred despite very high levels (over 98%) of immunization, and transmission was documented among appropriately immunized persons, ie those immunized at 12 months of age or above (Davis et al, 1987). Several outbreak investigations assessed risk factors for measles disease; those identified included immunization between 12 and 14 months of age, immunization before 1979 (independent of age at immunization), lack of provider verification of school records (Markowitz et al, 1989), and behavioural factors increasing the potential for measles transmission, such as attendance at basketball games (Davis et al 1987).

In response to these school-age outbreaks, the Immunization Practices Advisory Committee (ACIP) in 1989 recommended more aggressive outbreak control measures. During school- or college-based outbreaks, all students whose most recent dose of vaccine was prior to 1980 were to be reimmunized. In preschool outbreaks, the previous recommendation of lowering the age at immunization to 6 months, with reimmunization at 15 months of age, continued. These measures proved disruptive and costly to implement, and measles incidence continued to rise in 1988 and the first half of 1989. Currently, a recommendation for a

routine two-dose schedule, the first dose at 15 months of age and the second at school entry, is under consideration, in addition to universal reimmunization during outbreaks.

In the UK, measles immunization was not as aggressively implemented as in the USA. The pre-immunization pattern of biennial measles epidemics was changed to smaller, more frequent epidemic peaks (Fig 3) (Fine and Clarkson 1982b). There has been only a slight change in age distribution, the mean age at infection increasing from 4.3 to 5.3 years (Anderson and May 1985).

2.2.2 Developing countries

Measles immunization was first introduced into many developing countries as part of the smallpox eradication campaigns in the late 1960's. The campaigns dramatically reduced measles incidence in many countries, but rebounds in incidence quickly followed (Foster and Pifer 1971, Guyer 1976, Mitchell 1985). In a low population density province of Nigeria, high coverage was achieved in a 2 month period, and measles incidence remained low for about two years. In high density urban areas, such as Western Nigeria, lower coverage (65-81%) was achieved and the campaign took 18 months to complete. Reported cases fell to about 50% of normal, but incidence rose again after one year (Fig 4) (Smith and Foster 1970b). A model developed by Macdonald predicted that measles immunization campaigns in West Africa would have to be repeated at least annually to prevent epidemic disease.

Guyer and McBean (1981) found that a large proportion of vaccine was wasted in the maintenance campaigns in Cameroun. Campaigns were often held just after the epidemic season, rather than before; more than 80% of vaccine doses were given to children already immune or the vaccine had lost potency prior to injection; and the major maternal and child health centre programme attempted to vaccinate children at both 6 and 12 months of age, so that only about half the six month olds were protected, and few children returned for the second dose.

Following the smallpox eradication campaigns, measles immunization became integrated in the routine health services in sub-Saharan Africa. It has been included in the EPI more recently in Asia.

One of the problems of measles immunization in developing countries is the "window" problem (Mclean and Anderson 1988a). Most children are born with maternally derived antibodies, which persist for 3-12 months and, until recently, have prevented successful immunization. At the same time, behavioural and demographic factors in developing countries lead to high transmission rates and infection of children soon after they lose maternal antibodies. Thus if immunization is withheld until most children have lost maternal antibodies, a substantial proportion of a cohort will already have contracted measles, especially in densely populated areas. This is in contrast to the situation

in developed countries, where the average age of infection is about six years and there is a "window" during the second year of life, before the period of high measles transmission, when virtually all children have lost maternal antibodies and can be immunized successfully.

The "window problem" in developing countries led to controversy over the optimum age to immunize against measles. Due to the high incidence of measles in infants, measles vaccine was initially applied at 6 months of age, but low seroconversion rates were reported. Some countries tried two-dose immunization programmes, but found an unacceptably high dropout before the second dose (Guyer and McBean, 1981, Heymann et al 1983). Based on serological and epidemiological studies in Kenya and in Latin America, predictions were made of the number of cases and deaths avoided by immunization at different ages. These estimates showed that maximum benefit would be obtained by immunization at 8-10 months of age, and WHO recommended a single dose of measles vaccine at 9 months of age.

Initially it was expected that by immunizing a high enough proportion of 9 month olds, measles transmission would be sufficiently decreased that younger infants would be protected by herd immunity. Experience in Yaounde seemed to support this prediction. In 1979, with measles vaccine coverage among children 12-23 months of age at 40%, there was a 44% decrease in reported measles among children of all ages, including a 64% decrease in the measles attack rate among children under the age of 9 months (Heymann et al 1983). However, other countries have not shown the same effect, and in urban areas, even at higher coverage rates, measles in children under 9 months remains a major problem (Dabis et al 1988, Taylor et al 1988).

Some countries in sub-saharan Africa which have achieved and sustained high coverage rates have recently reported outbreaks or an increase in the proportion of cases in children outside the current target age group (Table 5). The effect of moderate-to-high coverage is different in large urban areas than in areas with a predominantly rural, dispersed population. In the former, the main problem is endemic measles in children under 9 months of age. Few children remain susceptible by school age. In rural, dispersed populations, measles in school-aged children is growing in importance and sporadic outbreaks occur. In areas intermediate between these demographic extremes, measles outbreaks are occurring in both children under nine months old and in children over 2 years old, up to and including school-aged children.

Table 5: Measles epidemiology in countries with medium-to-high vaccine coverage, in sub-saharan Africa

Country or city	Total pop(1)	Yr EPI began(2)	VC (3)	VC>50% since(4)	Age-distribution(5) %<9m	%0-4 yr	School outbr(6)
Burundi	5	1980	57	1986	24 (7)	65	Yes
Swaziland	0.7	1980	74	1986	18	66	Yes
Lesotho	1.5	1980	78	1982	6	40	Yes
Malawi	8	1980	70	1982	36	85	No
Kinshasa	4	1976	82	1981	33	94	No
Maputo	1	1980	86	1983	20	60	No

Notes
1. Approximate population in millions
2. Year when immunization became part of routine health services
3. Vaccine coverage in children aged 12 to 23 months, measured in the most recent cluster survey, including history of immunization for children without documentation.
4. Year since when measles vaccine coverage has been over 50%.
5. Age-distribution = percentage of reported measles cases in each age group.
6. School outbr. = school outbreaks reported.
7. 0-11 months

Measles remains endemic in cities in Zaire, the Congo and Mozambique, which have coverage levels of over 58%. A large proportion of cases are in children under 9 months of age. In Kinshasa, Zaire, (population almost 4 million), 33% of cases reported between 1981 and 1987 were in children under 9 months of age, with no apparent change in the age distribution of reported cases over this period (Cutts 1988). A community survey in 1983 showed that age-specific attack rates were highest in children aged 6 to 11 months (Taylor et al 1988). In Pointe-Noire, the Congo, (population 300,000), 17% of cases hospitalized in 1985 were aged under 9 months. A community study in 1985 showed highest attack rates in children aged 12 to 23 months (Dabis et al 1988). In Pointe Noire and in some Mozambican cities, there has been an increase in the proportion of reported cases occurring in children over 2 years of age. However, case-fatality ratios are higher in younger children, and there have been no reports of major outbreaks among school-aged children.

2.3 Measles outbreaks in African countries with moderately high coverage

In Lesotho and Swaziland, both small countries with dispersed populations, there has been a marked increase in cases in older children. Measles vaccine coverage measured by cluster sample

surveys was 74% in Swaziland in 1987, and 78% in Lesotho in 1988. In Swaziland, 41%, and in Lesotho, 62% of cases seen in health facilities are in children 5 years or older (Foster 1988, Simpson 1989). Both countries have experienced small outbreaks in schools since 1987, though the attack rates have been low (5% in grades 1-3 in recent school outbreaks in Swaziland). A problem in both countries is the lack of documentation of vaccine status among school-children. In Swaziland, only 59% of a random sample of 280 school children gave a positive history of measles immunization or of measles. Nonetheless, 100% were seropositive for measles as measured by ELISA at the Centers for Disease Control, and most had high levels of antibodies (Simpson 1989).

In Burundi and Rwanda, countries with predominantly rural populations but high population density, recent outbreaks have occurred among both schoolchildren and preschool children. In Burundi, outbreaks occurred in 1988-9 in Muyinga health sector, which has a measles vaccine coverage of approximately 65%, estimated from routine data. Measles incidence had been low in Muyinga since a previous epidemic in 1980; the sector had been relatively spared during national epidemics in 1983 and 1986.

An investigation in one primary school in Burundi suggested that school children were an important source of infection for younger siblings. Twenty-eight cases occurred among 299 students in grades 1-5 (attack rate 9%). Twenty-five of the cases were the primary cases in their household, and they gave rise to 31 secondary cases, 90% of which were in younger siblings (Chen 1989).

A case control study conducted in four health centres in Muyinga failed to show an increased history of attendance at a health centre in the previous month for measles cases compared to controls presenting with other symptoms; thus nosocomial transmission did not appear to be important in this rural outbreak.

A community survey of 1902 children under five years old was conducted in the five most-affected villages in Muyinga, at the end of the outbreak in January 1989. Case-fatality ratios were not calculated directly, since information on the date of death was not collected, but excess mortality was calculated for children with a history of measles during the outbreak compared to children without such a history. Overall excess mortality was low : 2.1% (12/297 in the measles group and 28/1465 in the non-measles group). Excess mortality was 2.3% among unimmunized children and 0.3% among immunized children with measles.

In Rwanda, outbreaks occurred in three regions in 1989. Most cases occurred among children over 5 years old, but case-fatality ratios were highest in under-two year olds (Table 6) (Weierbach 1989). No details are available about measles transmission in schools.

Table 6: Reported case-fatality ratios, Byumba region, Rwanda 1989

Age (months)	Cases N	Cases %	Deaths N	Deaths %	CFR %
0-8	135	9.2	4	28.6	3.0
9-23	210	14.3	3	21.4	1.4
24-59	279	19.0	3	21.4	1.0
60 +	846	57.5	4	28.6	0.5
Total	1470	100.0	14	100.0	1.0

This outbreak had a relative excess of cases reported in children 5 years old and above (58%) compared with the national figures for 1988 (Table 7).

Table 7. Age distribution of reported measles cases and deaths, Rwanda 1988

Age (months)	Cases N	Cases %	Deaths N	Deaths %	CFR %
0-8	853	18.8	35	36.8	4.1
9-23	1060	23.4	33	34.7	3.1
24-59	1219	26.9	18	19.0	1.5
60 +	1403	30.9	9	9.5	0.6
Total	4535	100.0	95	100.0	2.1

The outbreaks in these countries occurred against a background of an overall decrease in morbidity and mortality (Figs 5-7). In Burundi, reported morbidity and mortality rates decreased by over 50% from 14.1/1000 population in 1981 (coverage 24%) to 6.2/1000 population in 1988 (coverage 56%). Mortality rates were 18/100,000 in 1980 and 8/100,000 in 1988. In Rwanda, reported incidence decreased by 97% from 15.1/1000 pre-immunization to 0.6/1000 in 1988, when coverage was 86%. Reported mortality decreased from 12.6/100,000 in 1980 to 1.4/100,000 in 1988.

2.3.1 Concerns about outbreaks in older children

Measles in older children has usually been reported to be less serious than in young children, so that the shift in age distribution from young to older children is a positive result of immunization, in terms of measles mortality. However, outbreaks among school-age children are of concern because of their potential to:

1. Result in loss of confidence in the immunization programme. Outbreaks are occurring at a time when measles vaccine coverage is high, and they follow years of low incidence. Mothers and health workers expect that measles will be prevented, hence strong social and political pressure may be generated when outbreaks occur (Chen 1989).

2. Lead to the infection of younger, more vulnerable children. In community studies in Guatemala, Gordon et al (1965) found that when the primary case was less than 5 years old, the secondary attack rate was lower than when the primary case was a child of school age (40% and 70% respectively). Epidemics of school origin had a more abrupt rise and fall in cases than those of preschool origin, due to the rapid spread of infection among school children and prompt extension from them to preschool children in the families involved.

3. Be associated with an increased case-fatality ratio, even among older children, due to the high number of secondary cases (Aaby, 1988b).

4. Divert resources from ongoing routine immunization services. Outbreak control activities are costly and time-consuming. If epidemic control efforts are not adequately planned, vaccine supplies can be quickly exhausted in immunizing older children, and countries can have difficulty in avoiding a stock break.

3. The effect of immunization programmes predicted by mathematical models

Mathematical models have contributed to the understanding of herd immunity, seasonal patterns of infection, and the effects of immunization programmes on measles. They have also been used to predict the effect of different strategies for measles control under different socio-demographic conditions. A short review of major findings from mathematical models is presented here.

3.1 Herd immunity (Fox et al 1971).

The concept of herd immunity refers to the "resistance of a group to attack by a disease to which a large proportion of the members are immune, thus lessening the likelihood of a patient with a disease coming into contact with a susceptible individual". Early attempts were made to predict the proportion of a population which should be immunized in order that unimmunized persons would not come into contact with a case of measles should it occur, and which would thus stop measles transmission. However, it was soon realised that the concept of herd immunity is directly applicable only to randomly mixing populations. Open populations are not randomly mixing, but are made up of many interlocking subgroups, such as families, schools, ethnic and socioeconomic subgroups, which differ in respect to the proportion of immunes and intimacy of contact. That is, neither immunity nor contact rates between individuals are randomly spread through a population.

Fox et al (1971) showed that for a given infectious agent, epidemic potential is determined by the number of susceptibles and the nature and frequency of their contacts with each other.

If these characteristics of the population are constant, other characteristics such as the size of the total population and the proportion immune have no influence on the epidemic potential. The question "what proportion of the population should be immunized in order to prevent an epidemic" cannot be answered in absolute terms. The optimum immunization programme is one which reduces the supply of susceptibles in all subgroups. No matter how high the proportion of immunes in the total population, if some pockets of the community contain a large enough number of susceptibles among whom contacts are frequent, the epidemic potential in these pockets will remain high. This is clearly demonstrated by the occurrence of measles outbreaks in schools with high overall immunity levels in the USA, or among sectors of the community with religious exemptions to immunization (Novotny et al 1988).

3.2 Factors underlying seasonal patterns of measles incidence

In large unimmunized populations, measles epidemics occur at regular intervals. The progress of an epidemic is regulated by the number of susceptibles and the contact rates between infectious cases and susceptibles (Serfling 1952). In a given population, an increase in the number of persons susceptible to infection or in the frequency of contact between infectious individuals and susceptibles will lead to an increase in measles incidence. Measles incidence will continue to rise, thus reducing the number of persons susceptible to measles, until the chance of an infectious person making contact with a susceptible person decreases, when measles incidence will begin to fall. As measles incidence falls, the number of susceptibles will rise again, until a "threshold density" of susceptibles is passed, at which measles transmission increases and incidence rises.

A rise and fall (oscillation) in measles incidence around the "threshold density" of susceptibles may occur due to chance (stochastic) variations in the entry of susceptibles to the population or in the frequency of contact between susceptibles and infectious persons. In this case, one would expect the measles incidence to oscillate randomly and gradually to approach a constant. The consistent, regular pattern of measles epidemics argues for the existence of underlying factors other than random variation which change either the density of susceptibles or contact rates.

Fine and Clarkson (1982a) analysed patterns of measles transmission in England and Wales in the pre- and post-immunization eras. They used a simple mass action principle to estimate the number of cases of measles in a subsequent time period (C(t+1)) as the product of the number of current cases (Ct) and of current susceptibles (St), multiplied by a proportionality factor, Rt, which they termed the "transmission parameter". They calculated the transmission parameter by calendar week, using the model C(t+1)=Ct*St*Rt, and compared it to the weekly notifications of measles and the weekly number of susceptibles, estimated by cohort analysis. Figure 8 shows the results from the model.

Trends in the transmission parameter were similar in high and low incidence years, showing that the difference in incidence between years was caused by differences in the number of susceptibles. The transmission parameter fell during school holidays, and rose after school opening, being followed by a rise in disease notifications. The introduction of widespread immunization did not change the effect of school terms on the transmission factor, and hence on measles incidence, but the previous regular biennial pattern of high and low measles incidence was lost.

3.3 The effect of widespread immunization on measles incidence

Immunization programmes which immunize a portion of the birth cohort each year slow the rate of entry of new susceptibles into the population and hence slow the rate of transmission of measles. This has two effects: lengthening the interepidemic interval and shifting the age distribution of measles towards older children.

3.3.1 Changes in the age distribution of cases

In the absence of immunization, the age distribution of cases is determined by the rate of maternal antibody loss and the age-dependant forces of infection (the latter are in turn determined by age-related changes in frequency of contact with other persons).

Immunization acts to reduce the net rate of transmission within a population and thus tends to increase the average age at infection. The relationship between the average age at infection and the level of immunization coverage is non-linear; the initial change in average age at infection is slow, but it increases rapidly as very high coverage levels are reached. Though the proportion of cases in older children increases after immunization, the absolute number of such cases may fall, due to the overall reduced incidence rate of measles.

Fine and Clarkson (1982b) estimated age-specific prevalence rates of immunity, due either to natural infection or to immunization, for successive birth cohorts in England and Wales since 1950. The immunization programme, begun in 1968, raised the immunity levels of the younger age groups. However, there was a progressive fall in immunity levels in the older age groups, who were persons born during the period 1955-1965. These persons were too old to have been immunized but had escaped measles due to the general decline in incidence rates in the community in the post-immunization era. In the cohorts born before 1956, most individuals had contracted measles by their 16th birthday.

3.3.2 The "honeymoon" period

After immunization, the accumulation of susceptibles is slowed so that it takes longer for the epidemic threshold to be passed. However, the reduction in the number of young susceptibles is

balanced by the accumulation of older susceptibles as overall measles incidence is reduced and children who would previously have been infected by a certain age escape infection. Fine and Clarkson (1982b) showed that the net result of this shift (increased immunity in younger children and decreased immunity in older children) was that the total number of individuals susceptible in the population of England and Wales appeared to have remained relatively constant despite the immunization programme.

The period of low incidence following the introduction of widespread immunization (the honeymoon period) is generated during the shift from the pre-immunization to the post-immunization age distribution of susceptibles (McLean and Anderson 1988b). A gradual introduction of an immunization programme changes the age distribution of the susceptible population less. Rapid achievement of high coverage will induce a period of low incidence, after which the system settles to a higher level of incidence (but lower than that pre-immunization), with an inter-epidemic period longer than that pre-immunization. The higher the coverage achieved, the slower the accumulation of susceptibles, and the longer the inter-epidemic interval (figs 9,10).

Thus, a dramatic short-term reduction in measles incidence after the start of mass immunization is not an accurate reflection of long-term impact. This initial period will be followed by the recurrence of measles epidemics as measles incidence rises and falls around the new equilibrium.

3.4 Predictions of the effects of different strategies

Mclean and Anderson (1988a,b) modelled the effect of different immunization strategies on measles incidence and mortality rates to assess (1) the optimum age for measles immunization, (2) the impact of a two-stage immunization strategy, and (3) the impact of a two-phase immunization strategy.

3.4.1 The optimum age for measles immunization

The impact of 50% immunization on morbidity and mortality rates was estimated when vaccine is applied at different ages, for two communities:

a) a community with a mean age at infection of 1.09 years: data were taken from Dakar, Senegal pre-immunization. The mean duration of protection by maternal antibodies was set at 3 months, and 100% of 2 year olds were seropositive.

b) a community with a mean age at infection of 3.2 years, and mean duration of maternal antibody protection of 6 months. Data were taken from Bangkok, Thailand, pre-immunization.

Immunization was assumed to confer protection in each situation. The greatest reduction in morbidity and mortality was predicted to occur in community (a) when 6 or 9 month olds were immunized, and in community (b), when 18 month olds were immunized.

3.4.2 Two-phase immunization policies (immunizing at a young age in the early phases of an immunization programme with a subsequent change to an older age).

Previously it was expected that achieving high coverage at 9 months of age would reduce measles transmission in young children and allow a subsequent change in the age at immunization to 12 months or later, a time when all children have lost maternal antibodies and vaccine efficacy is higher (Black 1982). This assumption was based on the similarity of age distributions in developing countries having advanced immunization programmes to that in developed countries. However, the underlying epidemiology is different in the two situations. The patterns of age prevalence observed in developed countries are a consequence of low rates of transmission and low birth rates. In contrast, the age distributions in developing countries post-immunization are a consequence of the artificial reduction of the susceptible pool by immunization. If the age at immunization is increased, young children who are susceptible quickly accumulate, and epidemics can occur among them as they did pre-immunization. An unchanging one-stage strategy therefore results in lower morbidity and mortality than strategies with the same level of coverage which switch to immunizing older children.

3.4.3 Two-stage immunization regimens (immunization of half the population at a young age and half at an older age).

The effect of immunizing 75% of 9 month children was compared to that of immunizing 50% of 9 month olds and 50% of the remaining unimmunized children at an older age. That is, the total coverage was equal in the two strategies. The two-stage programme led to higher morbidity and mortality. Though no immunization programme would be likely to institute such a schedule deliberately, a similar situation would arise if compliance with immunization programmes were low, so that many children were not brought for immunization at the recommended age, but were immunized during visits to health services at an older age.

4. Lessons learnt and their operational significance for the improvement of measles control

1. Developing countries have high birth rates, high case-fatality ratios, early loss of maternal antibody, and high measles transmission rates, in comparison to developed countries. Though the age-distribution of measles cases in developing countries with advanced immunization programmes may resemble that of developed countries prior to immunization, recommendations on the age at immunization in developing countries should not necessarily be based on the experience in developed countries, since the age distribution in each instance is a function of different socio-demographic and epidemiological parameters.

2. A period of low incidence of infection is to be expected following the introduction of a mass immunization programme.

This will be followed be a new pattern of recurrent epidemics, with a lengthened inter-epidemic period. Intuitively, in urban areas epidemics will be more frequent than in rural areas, due to their high birth rate, high in-migration from surrounding areas, and high contact rate between susceptibles and infectious persons.

3. Estimates from mathematical models of the percentage immunization required to achieve herd immunity are guidelines only and do not imply that any one level of coverage will eliminate measles in all situations. Success of an immunization programme requires knowledge of the age and subgroup distribution of susceptibles and maximum effort to reduce their concentration throughout the community.

4. Outbreaks occur due to the accumulation of susceptible persons. The susceptible pool includes children too young to be immunized under the current schedule, children older than the target age group who were not vaccinated when they were eligible for vaccination and who have not been exposed to measles, children within the target age group who are unvaccinated, including temporary migrants, and vaccine failures. In developing countries, outbreaks currently occur principally among unvaccinated children, though the contribution of vaccine failures is difficult to assess due to poor documentation of immunization status. Vaccine failures may be expected among children immunized in the early years of the EPI, when a less heat-stable measles vaccine was used, but many of these children will already have acquired measles.

5. In large urban areas, even with high coverage with current vaccines, the number of susceptibles may always be enough to sustain transmission, so that measles remains endemic. For example, if coverage is 70%, the annual number of susceptibles entering the second year of life is at least 30% of the birth cohort, and may be as high as 44% if vaccine efficacy of Schwarz vaccine at 9 months of age is 80%-85% (EPI 1984, Hull et al 1983). The number of susceptibles is augmented by children who have lost maternal antibodies but have not yet reached the minimum age for immunization, who may be numerous in large areas with a high birth rate, and often also by unimmunized migrants from rural areas.

6. High coverage must be achieved soon after the age at which children become susceptible, to avert the maximum number of measles deaths. That is, after maternal antibody has waned and before many children have acquired measles. In much of sub-saharan Africa, this age is soon after 6 months (Black, 1982, Boue 1964, Taylor et al 1988).

5. Options to improve measles control in developing countries

North America, Europe and the Caribbean Region have goals of eliminating indigenous measles from countries in their regions. Strategies used include the achievement and maintenance of high coverage, improved disease surveillance, and aggressive outbreak control. In most developing countries, the current goal is not measles elimination, but measles control, and resource constraints are far greater. The applicability of potential additional strategies for measles control to developing countries is discussed here.

5.1 Achievement and maintenance of high coverage

Priority to measles control in urban areas is warranted because of the high mortality among young children who account for a greater proportion of cases in urban than rural areas, and to reduce transmission to rural areas (Davis 1982, Mitchell and Balfour 1985, Walsh 1983). Actions to increase coverage have been described by WHO (EPI 1985b). Three important actions are to avoid missed immunization opportunities, establish a system for detection and referral of defaulters from immunization, and identify pockets of low coverage.

As overall coverage increases, it becomes important to identify low-coverage areas. Estimates of coverage on a small-area basis can be made from routine data on the number of immunizations applied and the estimated target populations, or by the Lot Quality Sampling method (Lemeshow and Stroh 1988). Health services should be evaluated in the low-coverage areas to determine if the low coverage is due to non-availability of immunization, poor quality of the health services providing immunization, or poor acceptance by the community, and the appropriate response initiated.

In more remote rural areas where year-round immunization is not currently feasible, possibilities are to conduct periodic (at least annual) campaigns using mobile teams, or outreach immunization from district health centres. Outreach immunization, organised at district level in annual "pulses" has achieved sustained high coverage in rural areas of southern India (John et al 1980) and Mozambique (Cutts et al 1988).

If continuous immunization against measles is not feasible, measles immunization should if possible be timed for the seasonal trough in incidence, to try to prevent the accumulation of susceptibles over the threshold density. Increased incidence signifies that the transmission parameter and the number of susceptibles have already increased and control by immunization will be more difficult.

5.2 School-entry immunization

School-entry laws played a large role in increasing vaccine coverage in the USA, and have recently been instituted in many European countries (Noah 1987). In developing countries, cohorts

of incompletely immunized children from previous years of low coverage may be forming a pool of older susceptible children, especially in less densely populated areas where unimmunized children can survive to older ages without contracting measles. School entry screening and immunization is a potential means of conducting "catch-up" immunization of these children.

Major constraints on the widespread adoption of school entry screening and immunization in developing countries are the limited resources available, the low school enrollment in many areas of developing countries, and poor documentation of immunization status of school enterers. Though some countries already provide immunization services for primary school children (eg tetanus toxoid, BCG), for many countries school-entry immunization would require the establishment of new services, which could reduce the resources available for the under-two year olds. Identification of children susceptible to measles would be difficult since few children of school age have immunization cards, and histories of measles illness are inaccurate (Simpson 1989). An alternative would be to immunize all school enterers, without screening. However, since measles transmission in the under-fives remains high in densely populated areas of developing countries, most school children are likely to be immune, and much vaccine would be wasted if such a policy were adopted in all areas.

5.3 Aggressive outbreak control

In developed countries with aggressive outbreak control programmes, a single case of probable measles triggers outbreak investigation and control. This is only feasible in areas where measles is no longer endemic. Even restricting the definition of an outbreak to a cluster of related cases of over a given size, institution of aggressive outbreak control too soon in the development of an immunization programme could commit resources to this labour intensive activity, to the detriment of routine services. Surveillance and containment (ring immunization), which was a highly successful strategy for smallpox eradication, is not an alternative to sustaining high overall coverage rates for measles control, due to measles' high transmission rates, and the lack of a permanent marker of measles vaccination (Henderson 1982, Hinman et al 1987, Hopkins et al 1982). In the USA, even with a rapid, appropriate response from the health services, outbreaks have persisted among highly immunized school populations through several generations (Davis et al 1987, Wassilak et al 1985). Developing countries are unlikely to be able to respond quickly enough to interrupt transmission early in most outbreaks.

6. Conclusions and recommendations

The Expanded Programme on Immunization has made significant advances in reducing morbidity and mortality from measles. Some countries with moderately high coverage levels have reported outbreaks in children outside the current target age group for immunization. This is an expected consequence of an immunization programme whose target age group has been children under 2 years age. Another expected result of high coverage levels is an increase in the proportion (but not the rate) of cases which occur among children previously immunized (vaccine failures) (EPI 1985c, MMWR 1980, Orenstein et al 1985). Neither occurrence necessarily indicates programme failure. In countries currently reporting outbreaks in older children, the immunization programmes have succeeded in reducing overall incidence and mortality rates.

Examination of the data available to WHO as well as of theoretical predictions of the effect of immunization shows that the occurrence of measles in older children should not divert attention or resources from the need to increase coverage in young children. However, in many countries, immunization programmes have reduced measles incidence, so that health workers and the public expect measles not to occur. In such countries, outbreaks generate strong political and social pressure for response, and obviously cannot be ignored. Countries which have reached moderately high coverage levels should be aware that future outbreaks in older children may occur. They should maintain reserve stocks of measles vaccine so as not to jeopardise routine immunization of under-two year olds should an outbreak in older children occur.

Principal recommendations for developing countries are to increase coverage in young children and develop the capacity to respond to outbreaks.

6.1 Achieve and maintain high coverage

The current EPI recommendations for increasing coverage (EPI 1985c) remain of crucial importance to improving measles control. Priority should be given to urban and densely populated rural areas. Important measures to increase coverage are reemphasized here:

. Use all health centre contacts to immunize children.
  - Organize health centres to facilitate screening and immunization of all children attending for any reason.
  - Produce immunization cards in durable material and educate mothers to retain the immunization card and present it at any visit to a health centre.
  - Instruct health workers to open one vial even if only one child is to be immunized, and ensure that adequate stocks of vaccine are maintained.
  - Educate health workers about the lack of contra-indications to immunization. The following are NOT contraindications:

minor illness (fever, diarrhoea, cough etc)
HIV infection (symptomatic or asymptomatic)
exposure to measles illness

- Immunize children on admission to hospital if possible, or as soon as their general condition allows.

. Establish a system to detect and refer defaulters from immunization services.

. If special activities to increase measles immunization coverage are planned, such as immunization days or weeks, or outreach visits to rural areas, conduct them during the annual trough in measles incidence if possible.

. In areas where overall coverage is high (70% or above), identify pockets of low coverage and target activities to them.

. In areas where the private sector provides a large proportion of curative and/or preventive health services, involve the private sector in immunization activities.

. Though priority is given to urban and densely populated rural areas, conduct measles immunization at least annually in all rural areas, if resources permit.

. In areas experiencing increasing incidence among children over 2 years of age (outside the current target age group), consider immunization of previously unimmunized children in this age group when they attend health centres for other reasons.

6.2 Improve the health information system

Information on immunization coverage and on disease trends is important to :

- identify high-risk groups;
- monitor trends so that outbreaks can be anticipated;
- provide data to Ministries of Health, donors, and the public to show the progress made by the EPI;
- establish numerical targets for immunization activities and later for disease reduction;
- stimulate health workers to improve performance continuously.

Actions to improve the collection, analysis and use of data on coverage, measles morbidity and mortality are required at all levels of the health care system. Ideally, every health centre should be capable of monitoring outputs in comparison with the target population, and know the average number of measles cases seen per week, so that an increase in cases will be recognised and stimulate the appropriate response. The following are specific actions to improve the health information system.

6.2.1 Improve data collection

Coverage

Coverage surveys should be conducted regularly and comparisons made with routine data. Errors occur in coverage estimates obtained from data on the number of immunizations

performed and the estimated target population, due to inaccurate population estimates, immunization of temporary migrants who do not count in the denominator, and inaccurate registration of immunizations.

Disease surveillance

- Use a standard definition for measles diagnosis, eg the definition for suspect measles recommended by the EPI (Dondero 1984, Strassburg 1984):
  - A generalized rash lasting 3 or more days AND
  - Fever (38 degrees C. or more, if measured) AND
  - One of the following: cough, runny nose (coryza), red eyes (conjunctivitis).
- If data on measles incidence are not available through the routine health information system, conduct register reviews of hospitals and major health centres to establish trends in incidence, if possible by age group.
- Establish sentinel sites to obtain detailed age-specific data on measles incidence rates, case-fatality ratios, and the proportion of cases which occur in children previously immunized. Age-groups for reporting measles cases should be as narrow as possible; at a minimum, the category of "24 months and over" should be divided into two groups: "24-59 months, and 60+ months", to permit monitoring of an increase in cases among children of school age.

6.2.2 Improve data analysis

- Establish a system to analyse rapidly the incidence of measles by region.
- Monitor age-specific incidence rates and case-fatality ratios from sentinel site reports.
- Train peripheral health workers to:
  - compare monthly immunizations performed with the targets which have been assigned to them;
  - graph measles incidence;
  - tabulate cases (frequency and percentage) by age group;
  - tabulate cases (frequency and percentage) by immunization status.

6.2.3 Improve the use of data

- Provide verbal feedback on performance, including coverage and incidence results, during supervisory visits.
- Produce and distribute regular feedback bulletins.
- Liaise with administrative authorities and with the media to inform political leaders and the public of progress made by the EPI. Provide feedback on overall trends of measles, to show that overall incidence and mortality is less post-immunization than pre-immunization. In the absence of surveillance data showing impact of the immunization programme, estimate the number of cases and deaths averted from the estimated vaccine coverage and vaccine efficacy (Dondero 1984). Alert these groups to the possibility of

future outbreaks, which do not necessarily indicate programme failure.

- Educate health workers that a prolonged interval free from measles disease does not mean that control has been achieved. On the contrary, it is important to try to identify and immunize clusters of susceptible persons.
- Inform communities that outbreaks may occur if a sufficient number of unimmunized children accumulates. Enlist the cooperation of community leaders in detecting groups of susceptible persons.

6.3 Recognize and respond to outbreaks

The decision on when to respond to an outbreak depends on the previous incidence of measles in the area and the resources available. It is difficult to make a definition of an outbreak which applies to all situations. In rural areas where disease is not endemic, the first case usually marks the beginning of an outbreak (Gordon et al 1965), hence response should be immediate. In special situations such as refugee camps, where the potential for rapid and widespread transmission is great, rapid response to any measles case is also important. In areas where measles is endemic, there is no single definition of an outbreak. Each health area should try to determine the background incidence from previous years' data, and what "normal" seasonal variations are expected. A working guide is that if the present number of cases exceeds that in the same period in previous non-epidemic years, then further investigation is warranted, eg looking for clustering of cases which could signify the start of an outbreak (Strassburg 1984).

It is important not to disrupt routine services by attempts to control outbreaks. Recommendations for outbreak investigation and control are therefore divided into minimum actions indicated in areas with few resources, other actions which are ideal but not essential, and other non-essential investigations of interest. Each national programme should review its stage of development of immunization and determine how aggressively to promote outbreak control activities. A checklist of actions to take when an outbreak is suspected should be elaborated to aid peripheral health workers.

6.3.1 Priority actions

- Confirm the existence of an outbreak: the diagnosis of the disease, the location and number of cases, and the age groups affected.
- Review the data obtained on the age distribution of cases, to determine the upper age limit for immunization (the age at which a sharp drop in attack rates occurs or the age group affected by a previous epidemic). Estimate vaccine requirements and order the appropriate quantity of extra vaccine urgently, informing superior levels in the health system of the outbreak.

- Immunize all persons in the affected age group thought to be susceptible:
  - children without documentation of previous immunization at or after 9 months of age.
  - children with documented immunization if there is strong reason to believe that many vaccine failures have occurred (eg a known cold chain failure or use of expired vaccine).
- If the supply of vaccine is limited and the outbreak involves preschoolers with or without children of school age, give priority to immunizing children under two years of age.
- If a child has been exposed to measles, immunize and explain to the mother that the vaccine may not prevent infection since the child may be incubating the disease.
- Use all available communication channels to mobilize unimmunized children to attend for immunization. Enlisting the support of community leaders and the media is especially important if children outside the normal target age group are to be immunized.
- In high risk areas for vitamin A deficiency, treat cases with high-dose vitamin A (EPI Update 1988).
- Ideally, treatment should also be made available for measles cases. Outbreak investigation teams should include clinical staff and take essential drugs, eg Oral Rehydration Salts (ORS), anti-pyretics and antibiotics.
- A report of the outbreak investigation should be sent to higher levels of the health services system. Outbreak control activities should not be delayed while awaiting completion of the investigation.

6.3.2 <u>Optional additional activities to consider</u>

- <u>Lowering the age for immunization during an outbreak</u>

  In outbreaks which affect young children, the minimum age for immunization may be lowered to 6 months. The need for later reimmunization depends on the vaccine used: if vaccines become available which permit routine immunization at 6 months of age, there will be no change in the recommended age for immunization during an outbreak. Countries using the current, standard vaccines will need to reimmunize children whose first dose of measles vaccine was prior to nine months, as soon as possible after the child reaches 9 months of age. The use of such a schedule should be evaluated to determine what proportion of children return for a second dose. A concern is that if a large part of a country's immunizations are performed in response to outbreaks, then a high proportion of children will be immunized under the age of 9 months with standard-dose vaccines. If they do not receive a second dose, up to half of these children will not be protected.

- <u>School outbreaks</u>

  In school outbreaks, measles cases should ideally be excluded from school until one week after the onset of the

rash. Children without documented immunization should be excluded until they have received the vaccine. They can return to school immediately after having been immunized. Unimmunized siblings should also be immunized. Since a high degree of cooperation between health and education authorities, and good documentation of schoolchildren's immunization status are required to implement this recommendation, it may prove to be difficult in many developing countries.

. Ring immunization

A frequently cited recommendation is to conduct ring immunization around the affected area, such as was used in the control of smallpox. This strategy has not been adequately evaluated for measles control. Given the high transmissibility of measles, and the high degree of movement of many populations, it is difficult to implement. Long-distance travel means that it is difficult to define the radius to be included in "ring immunization".

. Outbreak control in urban areas

In urban areas, outbreaks do not occur in a circumscribed population, and infection is likely to spread throughout the city. It is difficult to distinguish between seasonal increases, or to decide if an increase in reported cases represents a normal "high incidence" year or not. Geographical clustering of the initial cases may help to decide whether an outbreak exists. If resources permit, house-to-house searches for unimmunized children can be conducted in the most affected areas.

6.3.3 Optional additional investigations

Outbreak investigation can provide further useful information on measles epidemiology. Possibilities are:

. Community-based surveys

Community-based surveys can provide more complete information on the age-distribution of cases and deaths, on age-specific attack rates and on acute and delayed mortality. Unless reports indicate that the outbreak is restricted to preschoolers, such investigations should include children up to the age of 10-15 years, or up to the age which first received measles vaccine, and not only the under-fives. This will allow the assessment of the importance of measles in older children. An example of a household investigation form is provided by Strassburg (1984).

. Studies of risk factors for disease

Studies of risk factors for disease, such as nosocomial transmission, or vaccine failure, may be easier to conduct

during an outbreak due to the large number of measles cases available. Protocols for the study of nosocomial transmission and of vaccine efficacy are available from EPI/Geneva.

- Studies of transmission patterns, eg from school-children to younger siblings, or from urban to rural areas.

- Documentation of the relative contribution of measles in school children to the overall burden of measles illness in the community.

- Evaluation of the cost-effectiveness of different outbreak response activities

6.4 Future policies

Immunization programmes in developing countries are increasing coverage rapidly, with the result that measles epidemiology is constantly changing. Strategies for measles control need to evolve as the EPI matures. New high-dose vaccines may make a one-dose schedule at 6 months of age a feasible option for many countries where measles in early childhood is common (Markowitz 1989). A routine two-dose schedule may be considered, to protect the small proportion of children who did not seroconvert after the first dose, to ensure lasting immunity, or to allow immunization of children under nine months of age until the newer generations of vaccines become widely available.

The USA is considering the introduction of a routine two dose schedule, in response to the problem of measles transmission among the small proportion of vaccine failures (Davis et al 1987, Markowitz et al 1989). Other countries with highly developed social services have achieved measles control through high coverage of preschool-age children and a two dose schedule (Bottiger et al 1987, Peltola et al 1986).

A two-dose schedule has most often been considered for developing countries for a different reason: to reduce the problem of measles in children under 9 months of age (Clements et al 1988, EPI 1986). The first dose could be applied at 6 months and the second at 9 months of age. Problems of low efficacy of the first dose and low coverage of the second dose, which occurred with this strategy in the 1970's, may be reduced by newer generations of vaccines which are more effective at 6 months, and by policies such as immunization at every opportunity, to reduce dropout between doses of vaccines (EPI 1989). A two dose schedule using standard vaccines is an option for countries where high-dose vaccines are not available, but further operational research to assess its impact and cost, ideally conducted in each area being considered, should precede any recommendations to introduce a two dose schedule for routine use in developing countries.

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<u>List of figures</u>

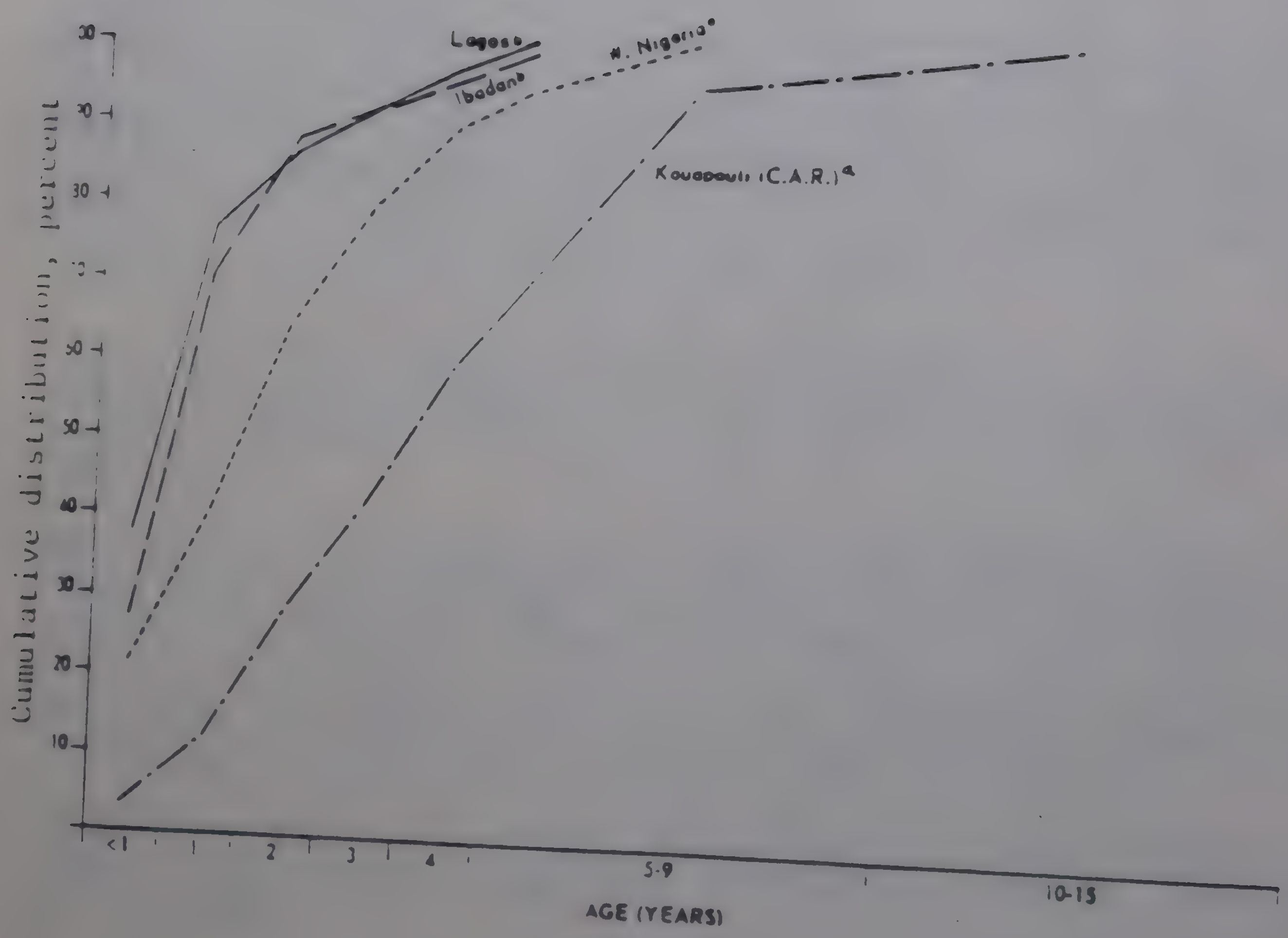


Fig 1. Percentage distribution of measles cases by age for four areas.
(a) : rural (b) : urban
After Foege, 1971

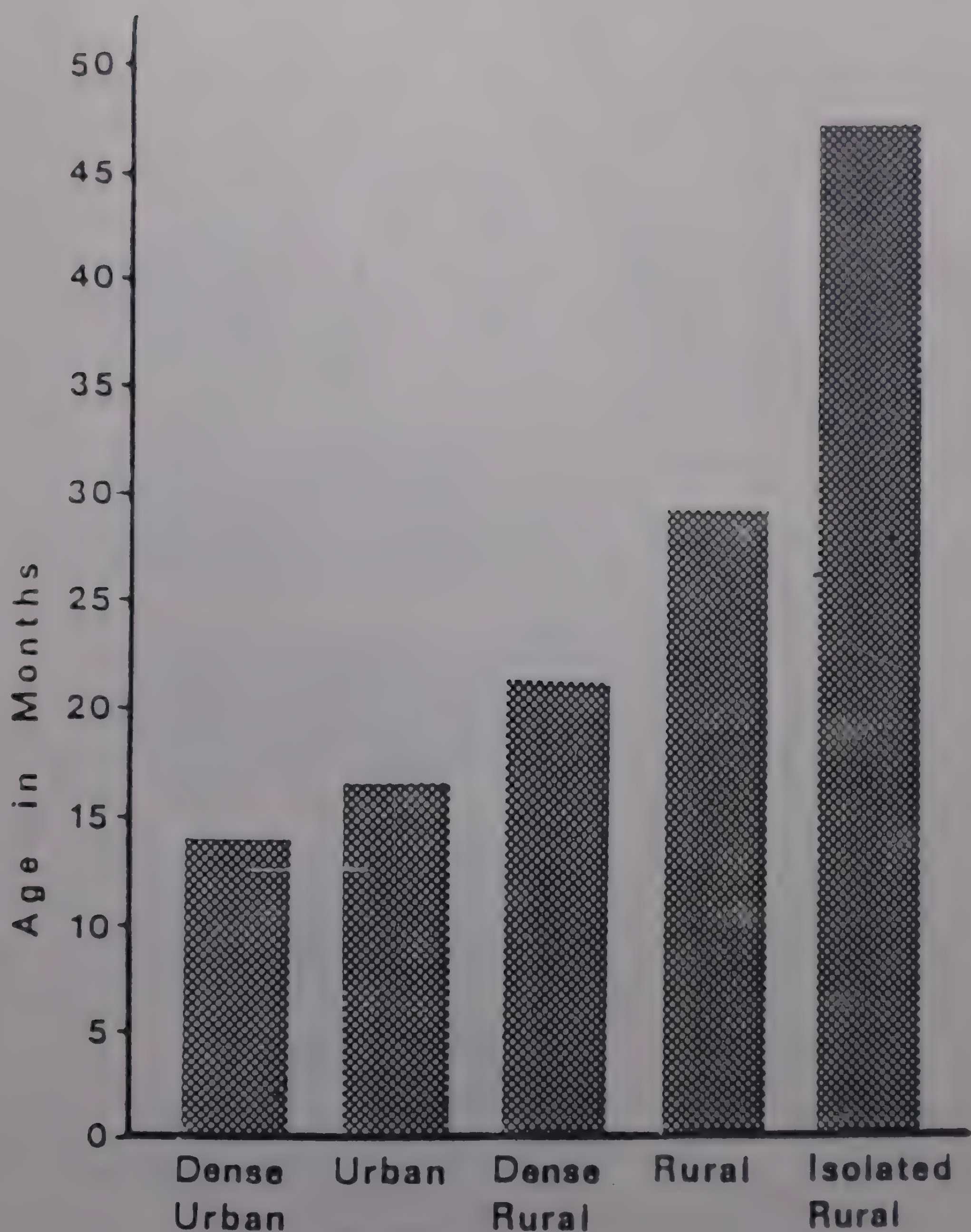


Fig 2. Median age of measles cases by urban-rural classification in West and Central Africa.

After Walsh, 1983

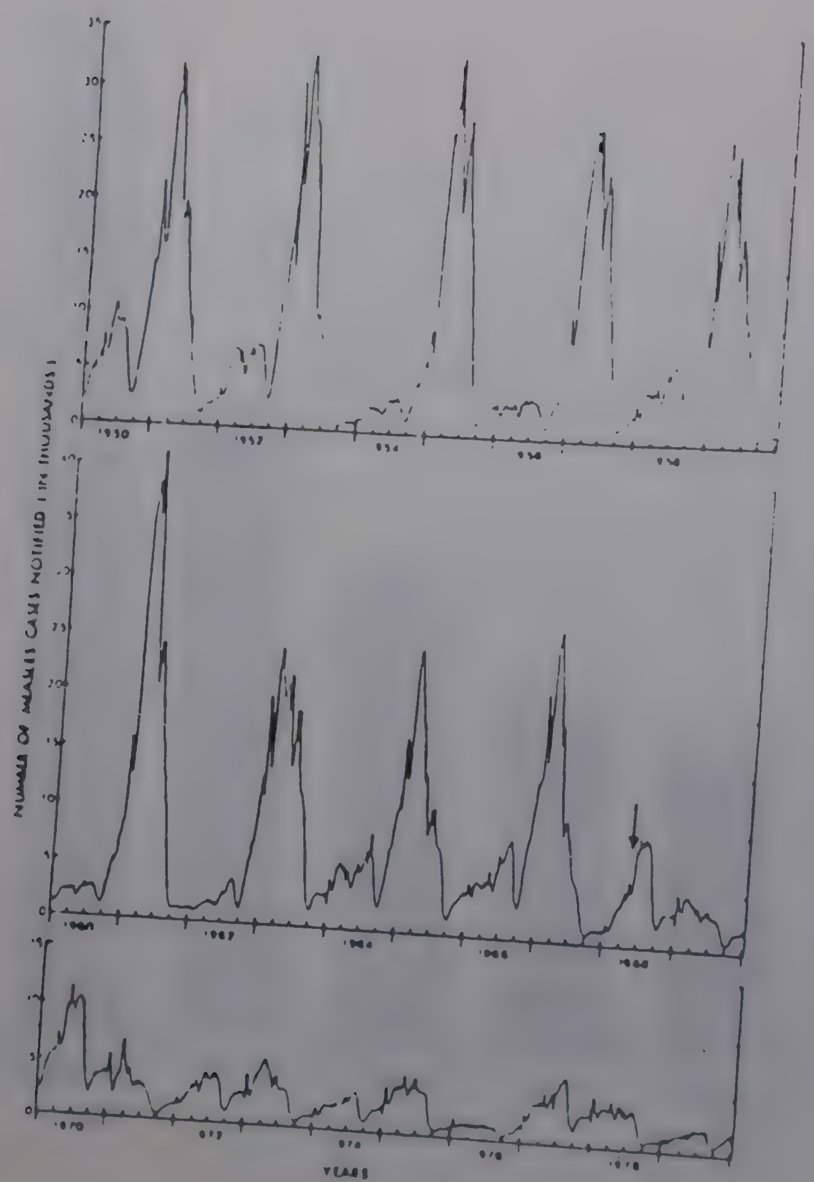


Fig 3. Measles notifications in England and Wales, by week, 1950-1979. The arrow indicates the beginning of the national measles immunization programme in 1968.

After Fine and Clarkson, 1982a

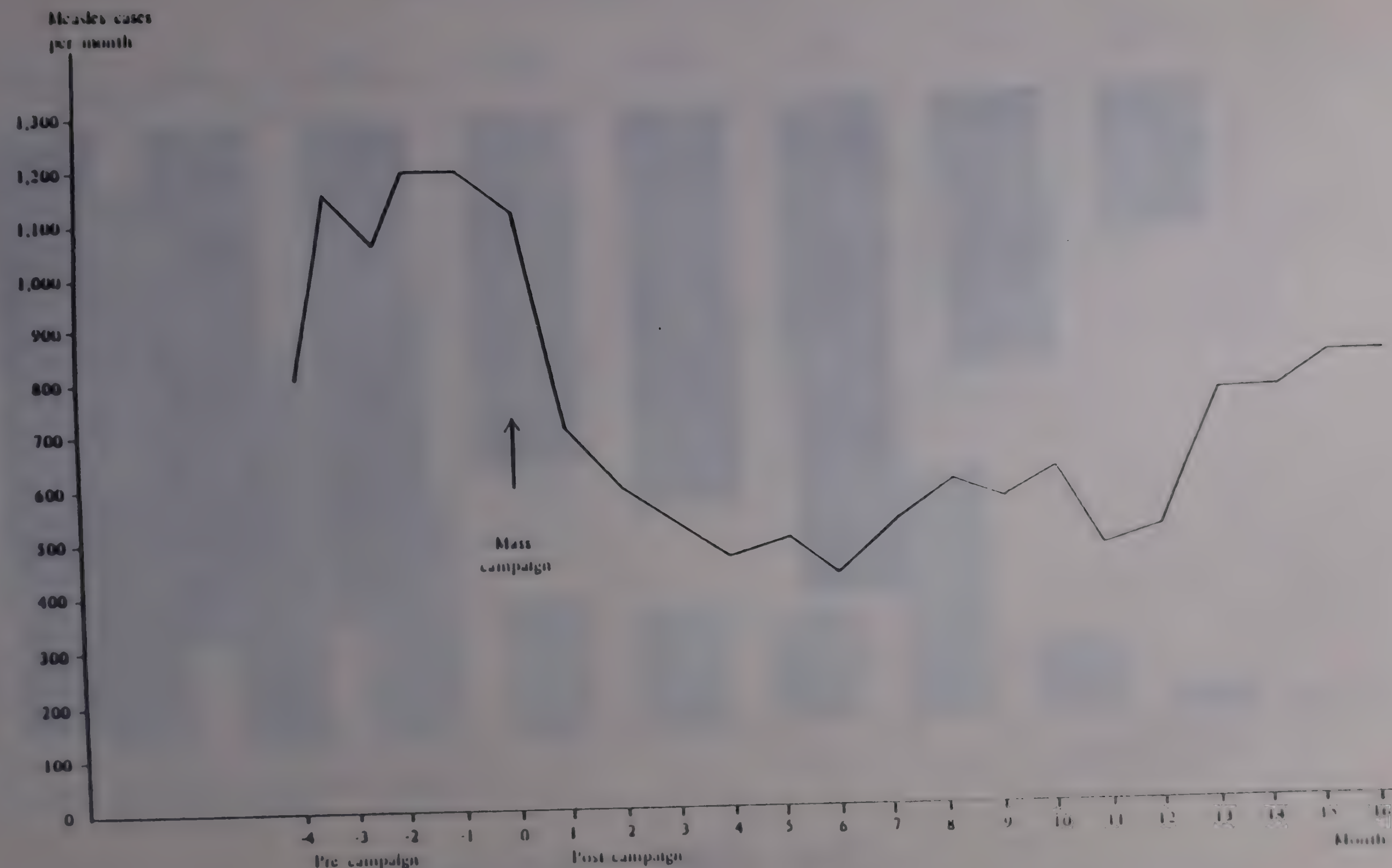


Fig 4. Measles cases pre and post measles campaign, Western Nigeria

After Smith and Foster, 1970b

Fig 5. MEASLES INCIDENCE AND VACCINE COVERAGE
LESOTHO 1980-1987

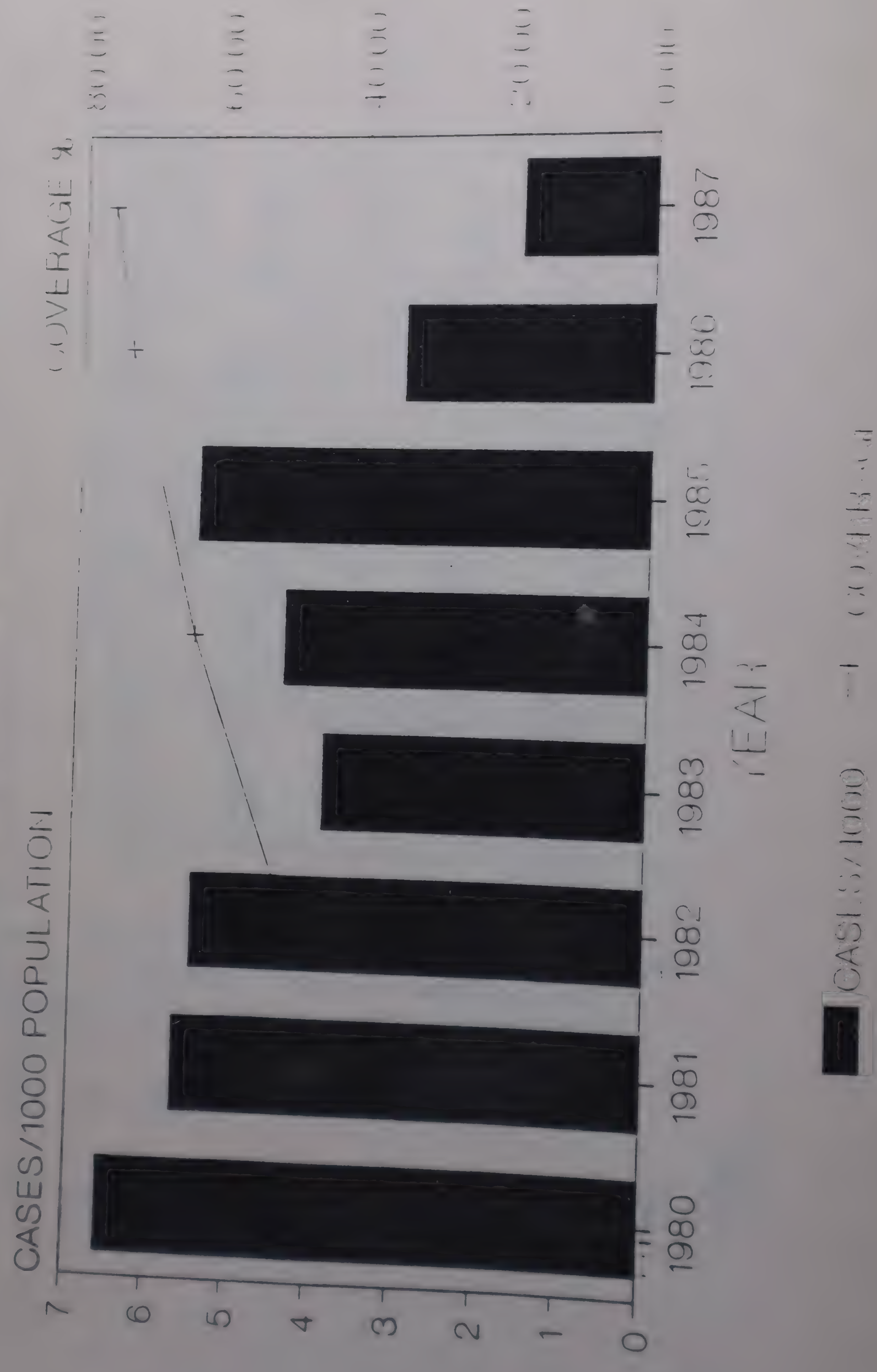


Fig 6. MEASLES INCIDENCE AND VACCINE COVERAGE
RWANDA 1980-1988

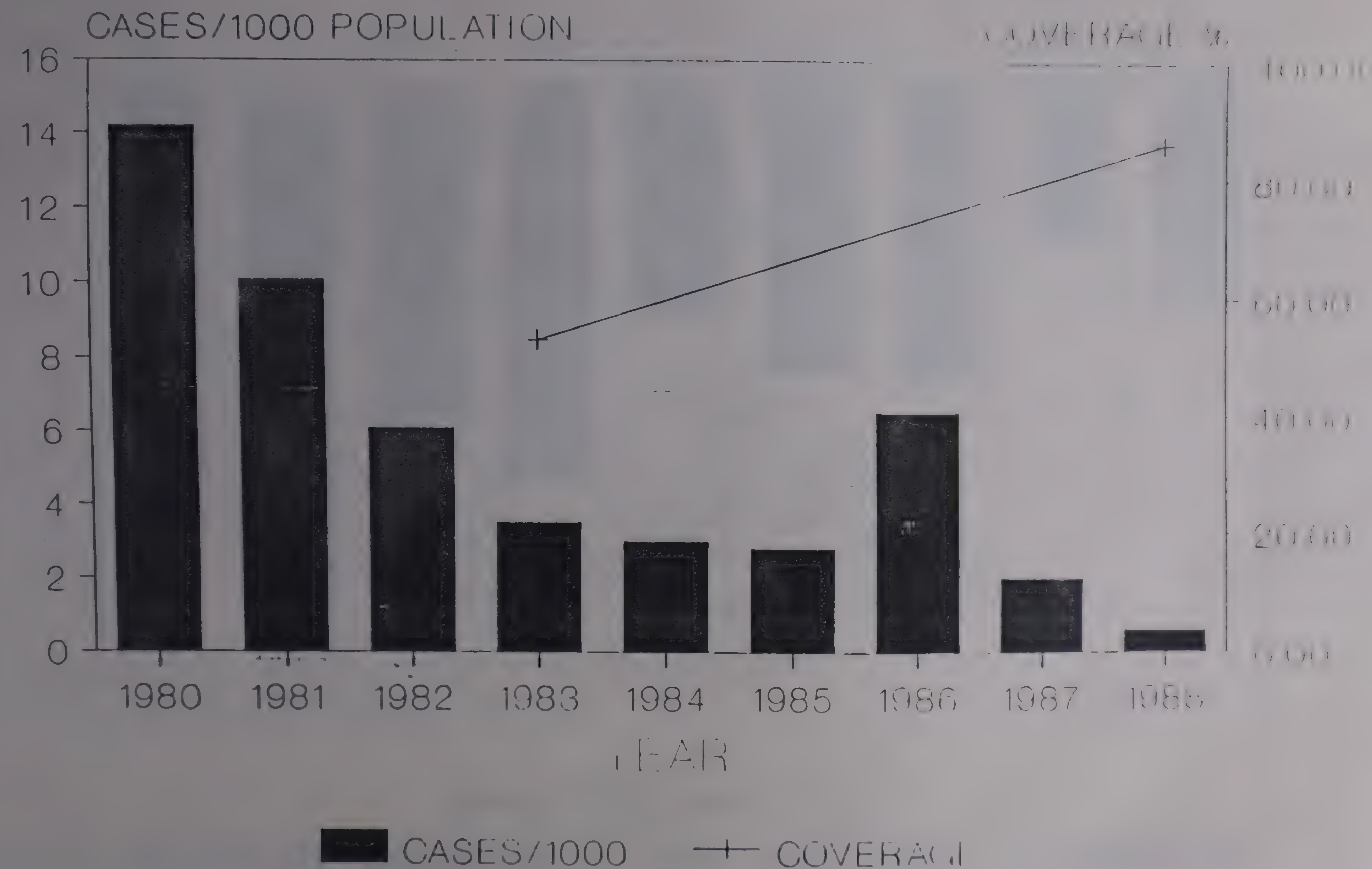
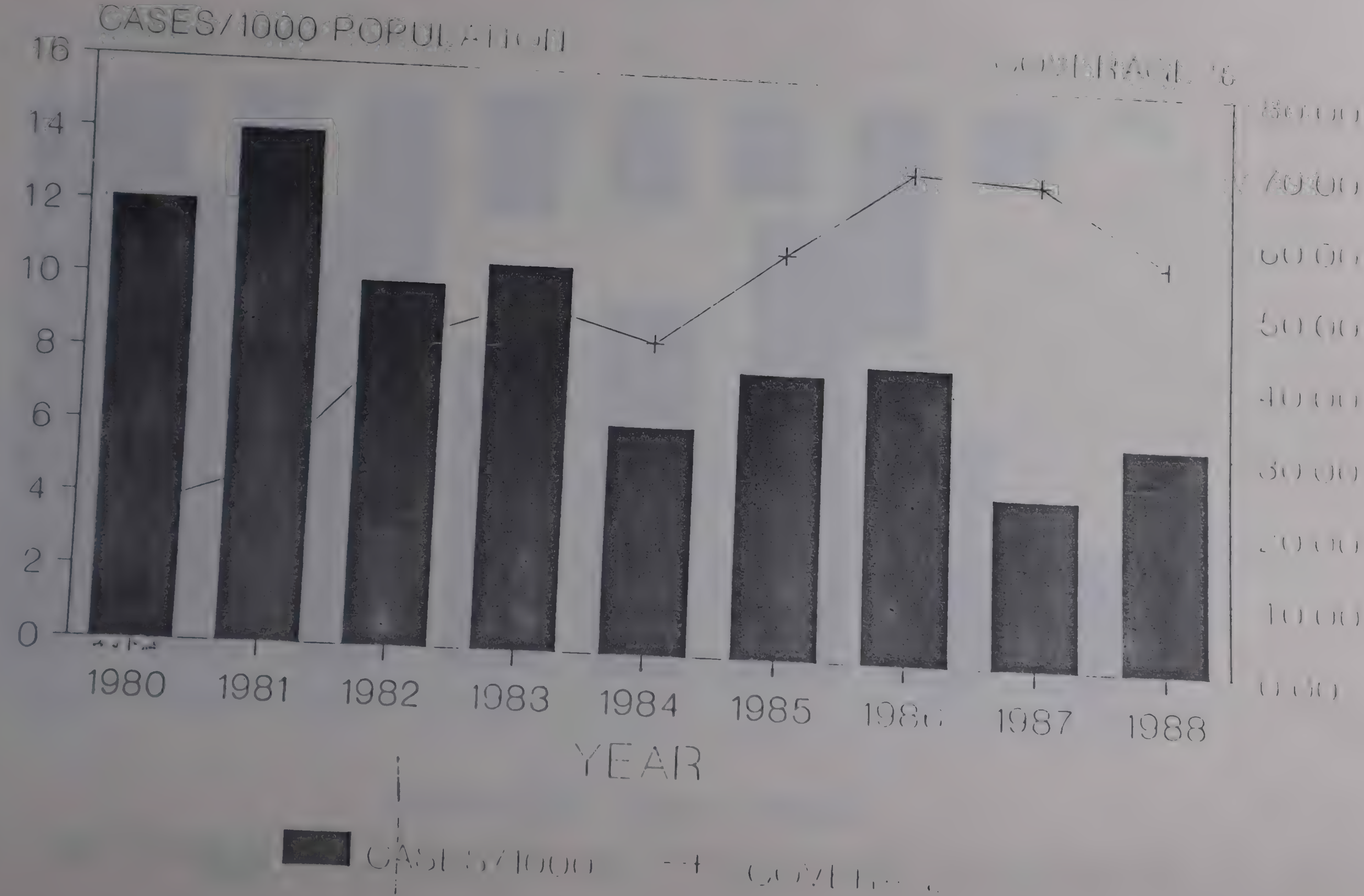


Fig 7. MEASLES INCIDENCE AND VACCINE COVERAGE BURUNDI 1980-1988



DATA FROM ROUTINE REPORT

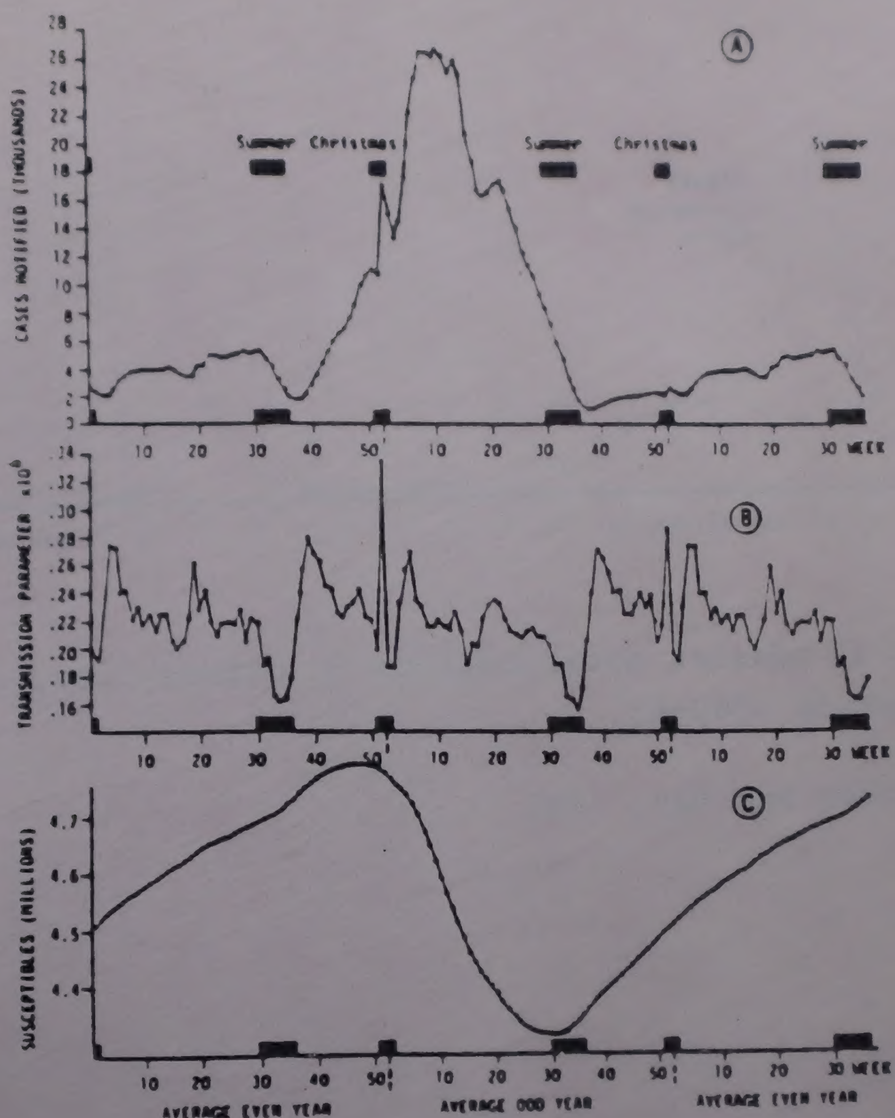


Fig 8. Analysis of average biennial measles pattern, based on data from 1950 to 1965.
(a) Average number of cases notified per week.
(b) Calculated weekly transmission parameters.
(c) Estimated number of susceptibles per week.
Shaded blocks indicate school summer and Christmas holiday periods.

After Fine and Clarkson, 1982a

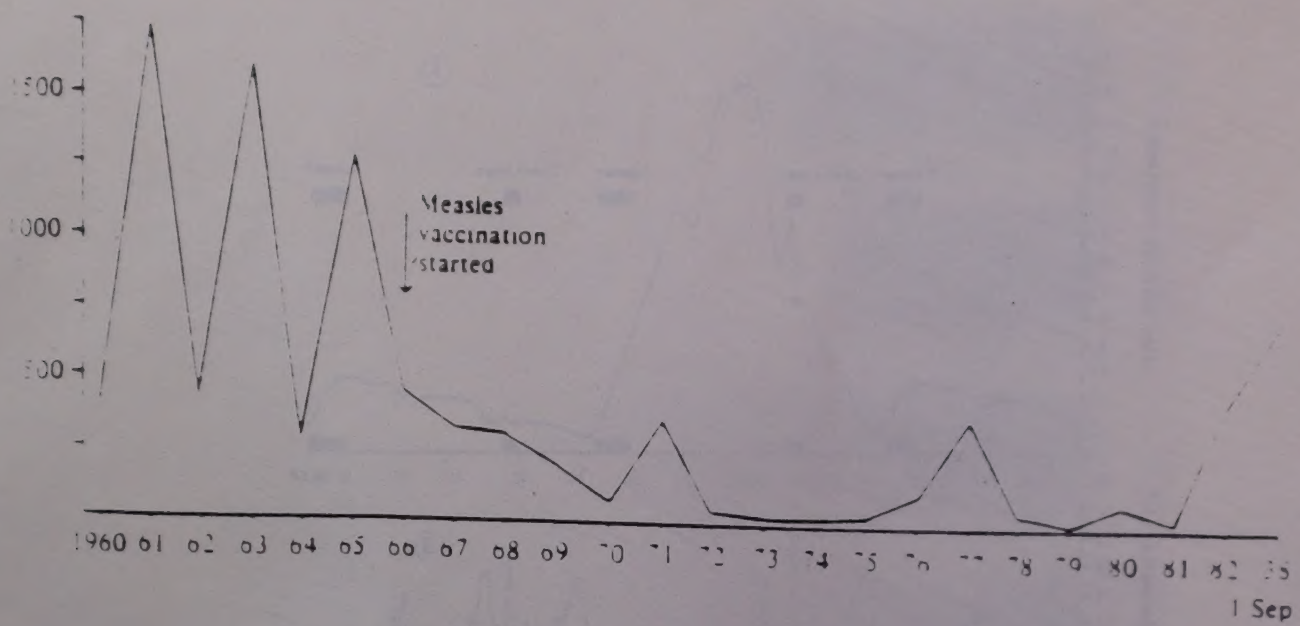


Fig 9. Annual measles notifications in Oxford City, England, over the period 1960-83.

After Anderson and May, 1985